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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/394,020	09/10/1999	CARMEN V. PEPICELLI	HUIP-P01-032	3626

28120 7590 03/22/2002

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EXAMINER
ANDRES, JANET L

ART UNIT	PAPER NUMBER
1646	

DATE MAILED: 03/22/2002

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/394,020	PEPICELLI ET AL.	
	Examiner	Art Unit	
	Janet L Andres	1646	

-- The MAILING DATE of this c mmunication appears n the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 February 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-15 and 22-32* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-15, 22-32* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

RESPONSE TO AMENDMENT

1. Applicant's amendment filed 25 February in paper no. 32 is acknowledged. Upon consideration, the finality of the previous office action is withdrawn. The text of those sections of Title 35, U.S. Code, not included in this action can be found in a prior office action.

Claim Rejections/Objections Withdrawn

2. The rejection of claims 16 and 17 under 35 U.S.C. 112, second paragraph, is withdrawn in response to Applicant's cancellation of these claims.

3. The rejection of claims 22 and 23 under 35 U.S.C. 112, first paragraph, is withdrawn in response to Applicant's amendment.

New Grounds of Rejection

Claim Rejections - 35 USC § 102

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

5. Claims 1, 3, 5, 25, and 26 are newly rejected under 35 U.S.C. 102(a) as being anticipated by Fujita et al., Biochem. Biophys. Res. Comm., Sept. 18, 1997, vol. 239, pages 658-664.

Fujita et al. teaches that human sonic hedgehog is expressed in squamous cell carcinomas and some adenocarcinomas (p. 658). Fujita et al. further teaches that an antibody to sonic hedgehog inhibits growth in these cells (Figure 5C, p. 662). Fujita et al. thus anticipates claims drawn to methods of inhibiting lung cancer cell growth using a hedgehog antibody. The effects

on downstream events as claimed in claim 26 would follow from the administration of the antibody.

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

7. Claims 2 and 4 are rejected under 35 U.S.C. 103(a) as being unpatentable over Fujita et al. Fujita et al. teaches as set forth above but fails to teach *in vivo* use. However, it would have been obvious to one of ordinary skill in the art to use an anti-hedgehog antibody to inhibit tumor growth *in vivo*. One of ordinary skill would be motivated to do so because Fujita et al. teaches that sonic hedgehog is expressed in squamous cell carcinomas and that an antibody to it inhibits proliferation of these carcinoma cells. Thus one of ordinary skill would conclude that an anti-hedgehog antibody could be used to inhibit tumor growth.

8. Claims 22, 23, 27, and 28 are rejected under 35 U.S.C. 103(a) as being unpatentable over Fujita et al. as applied to claims 1, 3, 5, 25, and 26 above, and further in view of U.S. patent

6261786, filed 2 July, 1996. Fujita et al. teaches as set forth above but fails to teach small organic molecules, as claimed in claims 22 and 23. Fujita et al. further fails to teach effectors of intracellular events, as claimed in claims 27 and 28. The '786 patent teaches small organic molecules in column 10, line 60. Modulation of intracellular events, as claimed in claim 27, is taught in column 52, lines 30-42. Inhibition of expression, as claimed in claim 28, is taught in column 28, lines 29-45. The '786 patent fails to teach inhibition of proliferation of lung cancer cells. However, it would be obvious to one of ordinary skill in the art to combine the teachings of Fujita et al. with those of the '786 patent to use small molecules or effectors of intracellular events in this way. One of ordinary skill would be motivated to do so because Fujita et al. teaches inhibition of proliferation by antagonizing hedgehog function, and the '786 patent teaches alternative methods of antagonizing hedgehog function.

Claim Rejections - 35 USC § 112

9. Claims 6-15, 24, and 29-32 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. These claims are drawn to methods of inhibition using N-terminal hedgehog molecules. However, the art (e.g. Fujita et al.) teaches that such N-terminal molecules are stimulatory. Thus, one of skill in the art would not predict that such molecules could be used as inhibitors. Applicant has provided no teachings or objective evidence to indicate that these molecules could b so used; what is set forth in the specification are the effects of a null mutation on development. Applicant's declaration of paper no. 28 does not remedy this defect; the nature of the antagonist is not specified. Thus, given that the art teaches away from the claimed method

and Applicant has not provided sufficient guidance to indicate which, if any, N-terminal molecules could be used, one of skill in the art would not predictably be able to use the invention as claimed. Thus, without further guidance predictive of such success, it would require undue experimentation for the skilled artisan to use the invention.

10. Claims 1-5 and 24-28 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for inhibition of lung cancer cell proliferation by antibodies and small molecules, as taught by the prior art, does not reasonably provide enablement for all methods of inhibition. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. These claims encompass all hedgehog antagonists. Applicant has set forth no examples of such antagonists in the specification and, as stated above, Applicant's declaration of paper no. 28 does not specify what antagonist is used. While the prior art teaches antibodies and screens for identifying other molecules, it does not teach N-terminal inhibitors, as set forth above, nor does it provide guidance for one of skill to identify the broad category of hedgehog antagonists. Without such guidance, one of skill could not predictably identify and use such inhibitors, and it would thus require undue experimentation for the skilled artisan to make and use the invention as broadly claimed.

NO CLAIM IS ALLOWED.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Janet Andres, Ph.D., whose telephone number is (703) 305-0557. The examiner can normally be reached on Monday through Friday from 8:00 am to 5:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler, Ph.D., can be reached at (703) 308-6564. The fax phone number for this group is (703) 872-9306 or (703) 872-9307 for after final communications.

Communications via internet mail regarding this application, other than those under U.S.C. 132 or which otherwise require a signature, may be used by the applicant and should be addressed to **[yvonne.eyler@uspto.gov]**.

All Internet email communications will be made of record in the application file. PTO employees do not engage in Internet communications where there exists a possibility that sensitive information could be identified or exchanged unless the record includes a properly signed express waiver of the confidentiality requirements of 35 U.S.C. 122. This is more clearly set forth in the Interim Internet Usage Policy published in the Official Gazette of the Patent and Trademark Office on February 25, 1997 at 1195 OG 89.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Janet Andres, Ph.D.
March 12, 2002

Yvonne Eyler
YVONNE EYLER, PH.D
SUPERVISORY PATENT EXAMINER
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